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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/183,375	10/30/1998	JANOS SZEBENI	003/098/SAP	3056

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Elizabeth A. Arwine (MCMR-JA)
Office of the Staff Judge Advocate
US Army Medical Research & Materiel Command
504 Scott Street
Fort Detrick, MD 21702-5012

EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
09/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/183,375	SZEBENI ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7-11,16-19 and 21* is/are pending in the application.

4a) Of the above claim(s) *7-9,11,18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,10,16,17 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment dated 7-27-07 is acknowledged.

Claims included in the prosecution are 1-4, 10, 16, 17 and 21.

In view of the amendments, the rejections involving the reference of Lodge have been withdrawn.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-4, 10, 16, 17 and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibition of complementation activation by sCR1, does not reasonably provide enablement for several inhibitors recited in the independent claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. It is well known that complement system is a complicated system and the activation of the complement can occur via at least two pathways: one involves antigen-antibody complexes. Applicant recites EGTA as one of the inhibitors. According to US 6,495,735, EGTA is a chelator, which removes calcium, which is essential for classical pathway complement activation, and so the presence of EGTA ensures that complement can only be activated by the alternative pathway (col. 14, lines 4-10). Applicant has not shown that all the inhibitors recited in the claims are able to inhibit the complement activation system, which is

activated by cremophor. For example, at least one of the inhibitors recited in the claims, zymosan is not an inhibitor at all and is recognized in the art as an activator (Ravetch et al, 5,877,396; col. 52, lines 25-30). Because the system is complex, one cannot predict based on the results obtained by one inhibitor that other inhibitors would also have the same effect. This is evident from the above-cited references. Broad claims must have broad basis of support in the specification; in the absence of such support, claims must be limited to the inhibitor, sCR1 which is shown to be effective against the side effects of cremophor.

> Applicant's arugments have been fully considered, but are not found to be persuasive. Applicant argues that it may only require routine experimentation to select the inhibitor from the claimed list and their use.

Although applicant simply deletes the compounds cited by the examiner as not being effective, the rejection is maintained since there is unpredictability in the art, as also recognized by applicant on page 7 first paragraph of the response; applicant has not shown that all the claimed inhibitors would be effective and it would require undue experimentation by one of ordinary skill in the art to determine which of the claimed inhibitors would be effective.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-4, 6, 10, 16-17 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Terwogt (cancer Treatment Reviews, March 1997) or O'Brien (Annals of Oncology, 1992) in view of Ko (5,851,528) and applicant's statements of prior art.

Terwogt teaches that that the antitumor drug paclitaxel is usually administered in combination with the vehicle, cremophor EL (polyethoxylated castor oil) and the administration of this combination causes severe hypersensitivity reactions (pages 88-89). What is lacking in Terwogt is the teaching of the administration of compliment activation inhibitors.

O'Brien teaches that several cytotoxic drugs including Taxol and doxorubicin cause hypersensitivity reactions (abstract and Table 2).

Ko teaches that compliment system includes a group of proteins in blood plasma, which plays an integral role in immune and allergic reaction and discloses a method of inhibiting complement activation by administering complement activation inhibitors. The method involves the administration of the inhibitor in controlled release delivery devices

such as liposomes. The method is used for various conditions including the drug induced allergies and inflammation (note the abstract, col. 3, lines 49-52, col. 5, lines 32-51, col. 11, lines 1-42, examples and claims). Ko is also suggestive of the administration of the inhibitor along with the drug from his statements on col. 10, line 42 et seq., according to which the inhibitor "can be combined with appropriate pharmaceutical formulation. Ko however, does not specifically teach instant drugs or carriers such as Cremophors. Ko does not teach claimed complement activator inhibitors. However, instant inhibitors are art known as evident from applicant's statements of prior art and therefore, one of ordinary skill in the art would ex

Applicant on page 22 indicates that the claimed inhibitors are known in the art.

In essence the reference of Terwogt shows the problems (hypersensitivity) associated with the commonly used drug-carrier (paclitaxel-Cremophor) combination and that of O'Brien shows that several drugs cause allergic (hypersensitivity) reactions. The reference of Ko offers a solution and applicant's statements of prior art indicate that the claimed inhibitors are art known.

To use complement activation inhibitors to reduce or inhibit the hypersensitivity reactions caused by paclitaxel-cremophor EL combination or that caused by drugs such as doxorubicin and others would have been obvious to one of ordinary skill in the art since Ko teaches that administration of complement activation inhibitor would reduce the allergies and inflammation caused by the drugs. To use art known inhibitors with a reasonable expectation of success would have been obvious to one of ordinary skill in the art since Ko teaches that a group of proteins play a role in the activation of the

complement system which includes immune and allergic reactions and is suggestive of that one such inhibitor is effective in alleviating various conditions. The criticality of the administration of the compliment activation inhibitor prior to the administration of the drug is unclear to the examiner since it would be obvious to one of ordinary skill in the art that such an administration would prevent the active agent or the carrier from activation of the compliment system. The criticality of the active agent in claim 17 is also unclear to the examiner since the claims are drawn to the inhibition of the hypersensitivity reactions by the compliment activation inhibitor and hemoglobin is known to be administered to anemic patients. Compliment inhibition by the inhibitor occurs irrespective of the nature of the drug.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that neither Terwogt and O'brien mentions compliment activation inhibitors or their use and that there is no suggestion of a relationship between complement system inhibition and the alleviation of the symptoms associated with hypersensitivity. The examiner agrees, but points out that Ko teaches the compliment activation system, the administration of the system inhibitors and the reference is suggestive of the administration of the inhibitor along with the drug. Applicant argues that Ko does not teach the treatment of hypersensitivity caused by cremophors. This argument is not persuasive since Terwogt teaches that cremophor causes the hypersensitivy reactions. Applicant argues that Ko does not teach the claimed compliment activation inhibitors. However, instant claimed inhibitors are art well known as applicant's statements of prior art indicates. Therefore, it would have been

obvious to one of ordinary skill in the art that instant inhibitors would inhibit the compliment activation system in a similar way as Ko's proteins (Supreme Court decision in KSR International Co. V. Teleflex Inc., 550 U.S. -, 82 USPQ2d 1385 (2007).

5. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Woodward Michael can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK